UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,515	08/07/2001	Rosanne M. Crooke	ISPH-0595	1714

36441 7590 09/22/2005

MARY E. BAK
HOWSON AND HOWSON, SPRING HOUSE CORPORATE CENTER
BOX 457
SPRING HOUSE, PA 19477

EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/923,515	CROOKE ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7,9,10,12,13 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7,9,10,12,13 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *July 5, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission mailed on July 5, 2005 has been entered.

Claims 1, 5, 7, 9, 10, 12, 13 and 15 are pending.

Claims 1, 5, 7, 9, 10, 12, 13 and 15 have been examined on the merits.

Response to Arguments

Applicants Amendment and Response mailed July 5, 2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed April 6, 2005 are hereby withdrawn. Any arguments addressing said rejections and/or objections are moot. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Information Disclosure Statement

Applicant's information disclosure statement filed July 5, 2005 is acknowledged. The references referred to therein have been considered on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 7, 9, 10, 12, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rouy et al. [WO 99/35241] in view of McLean et al. (Nature, 1987 Vol. 330:132-137), and Baracchini et al. [U.S. Patent No. 5,801,154].

Claim 1 is drawn to a non-cleaving antisense oligonucleotide 12 to 30 nucleobases in length and 100% complementary to a nucleic acid encoding human apolipoprotein (a) (SEQ ID NO:3), wherein said oligonucleotide specifically hybridizes

with said nucleic acid molecule and inhibits the expression of human apolipoprotein (a), and wherein said oligonucleotide comprises at least one modified internucleoside linkage, sugar moiety, or nucleobases. Claims 5, 7, 9, and 10 are dependent on claim 1 and include all the limitations of claim 1 with the further limitations wherein the modified internucleoside linkage is a phosphorothioate, wherein the modified sugar moiety is a 2'-O-methoxyethyl sugar moiety, wherein the modified nucleobases is a 5'-methylcytosine, and wherein the oligonucleotide of claim 1 is a chimeric oligonucleotide. Claims 12 and 13 are dependent on claim 1 and include all the limitations of claim 1 with the further limitations wherein the composition of claim 1 comprises a pharmaceutically acceptable carrier diluent and further comprises a colloidal dispersion system. Claim 14 is drawn to a method of inhibiting the expression of human apolipoprotein (a) in cells or tissues *in vitro* comprising contacting said cells or tissues with a non-cleaving antisense oligonucleotide 12 to 30 nucleobases in length and 100% complementary to a nucleic acid encoding human apolipoprotein (a) (SEQ ID NO:3).

Rouy et al. teach antisense nucleic acids that are capable of specifically hybridizing with a nucleic acid encoding apoliproprotein (a) and down regulating gene expression (see page 23, first full paragraph). Rouy et al. teach that preferably the antisense is at least 20 nucleobases in length (see page 23, first full paragraph). Rouy et al. also teach the antisense oligonucleotide can be modified to improve stability and specificity (see page 23, first full paragraph).

Rouy et al. do not teach a nucleic acid encoding apoliproprotein (a) (SEQ ID NO:3) and antisense nucleic acids comprising specific modifications (e.g. modified internucleoside linkage, modified sugar moiety, or modified nucleobases).

McLean et al. teach the full-length sequence of human apolipoprotein (a) (see Figure 1). It is noted that the full-length sequence taught by McLean et al. is 100% identical to SEQ ID NO:3 of the instant invention.

Baracchini et al. generically teach the design of antisense of 8 to 30 nucleobases in length and teach modifications to antisense, including 2'-O'methoxyethyl sugar modifications, 5-methylcytosine base modifications, chimeric oligonucleotides and modified internucleoside linkages, including phosphorothioate linkages, to increase antisense stability and enhance affinity (see for example columns 6-9). Baracchini et al. further teach pharmaceutical carriers and colloidal dispersion systems (for example liposomes) for use in delivery of antisense compounds.

It would have been obvious to one of ordinary skill in the art to make a non-cleaving antisense oligonucleotide targeted to a nucleic acid encoding apolipoprotein (a) (SEQ ID NO:3) using the motivation of Rouy et al. and the sequence taught by McLean et al. It would have been obvious to make a length within the range of 12 to 30 nucleobases since Rouy et al. taught preferably the antisense is at least 20 nucleobases in length and since Baracchini et al. explicitly taught the design of antisense oligonucleotides, 8 to 30 nucleobases in length, to a target gene of interest. One of ordinary skill in the art would have been motivated to modify the antisense to include 2'-O'methoxyethyl sugar modifications, 5-methylcytosine base modifications, or

phosphorothioate linkages because such modifications were routine and well known in the art as modifications which enhance the stability, uptake and affinity of an antisense molecule, (see for example, Baracchini et al. column 6, paragraph 3). One of ordinary skill in the art would have expected success in making a non-cleaving antisense oligonucleotide targeted to a nucleic acid encoding apolipoprotein (a) (SEQ ID NO:3) since Rouy et al. provide the motivation to do so, McLean et al. taught the sequence of SEQ ID NO:3 and Baracchini et al. taught that following generic teachings, the design and synthesis of modified antisense oligonucleotides to a target gene of interest can be made.

It would have been obvious to one of ordinary skill in the art to make a non-cleaving antisense oligonucleotide targeted to apolipoprotein (a) and a pharmaceutically acceptable carrier, including a colloidal dispersion system, because pharmaceutically acceptable carriers, including colloidal dispersion systems (e.g. liposomes) were well known in the art for use with antisense molecules as a means to deliver antisense molecules to cells *in vitro* (cell culture) (see Baracchini et al.).

It would have been obvious to one of ordinary skill in the art to use a non-cleaving antisense oligonucleotide in a method of inhibiting the expression of apolipoprotein (a) (SEQ ID NO:3) in cells *in vitro* since Rouy et al. taught antisense nucleic acids could be used to down regulate or block gene expression. One of ordinary skill in the art would have expected success to inhibit the expression of apolipoprotein (a) (SEQ ID NO:3) in cells or tissues *in vitro* because Baracchini et al.

taught that following generic teachings, one could use antisense oligonucleotides to inhibit the expression of a known target gene.

Therefore, the invention of claims 1, 5, 7, 9, 10, 12, 13 and 15 would have been obvious to one of ordinary skill in the art, as a whole, at the time the instant invention was made.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
September 7, 2005

ANDREW WANG
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600